DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

July 24, 2015

BIOPHOR DIAGNOSTICS, INC.
NATHANIEL BUTLIN
VICE PRESIDENT
1201 DOUGLAS AVE
REDWOOD CITY CA 94063

Re: K142129
Trade/Device Name: RapidFRET Oral Fluid Assay for Cocaine,
RapidFRET Oral Fluid Cocaine Calibrator Set,
RapidFRET Oral Fluid Cocaine Control Set
Regulation Number: 21 CFR 862.3250
Regulation Name: Cocaine and cocaine metabolite test system
Regulatory Class: II
Product Code: DIO, DLJ, DIF
Dated: July 1, 2015
Received: July 6, 2015

Dear Nathaniel Butlin:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration. Please note: CDRH does not evaluate information related to contract liability warranties. We remind you, however, that device labeling must be truthful and not misleading.

If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Parts 801 and 809); medical device reporting (reporting of medical device-related adverse events) (21 CFR 803); good manufacturing practice requirements as set forth in the quality systems (QS) regulation (21 CFR Part 820); and if applicable, the

electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.

If you desire specific advice for your device on our labeling regulations (21 CFR Parts 801 and 809), please contact the Division of Industry and Consumer Education at its toll-free number (800) 638 2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21 CFR Part 807.97). For questions regarding the reporting of adverse events under the MDR regulation (21 CFR Part 803), please go to http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm for the CDRH's Office of Surveillance and Biometrics/Division of Postmarket Surveillance.

You may obtain other general information on your responsibilities under the Act from the Division of Industry and Consumer Education at its toll-free number (800) 638-2041 or (301) 796-7100 or at its Internet address http://www.fda.gov/MedicalDevices/ResourcesforYou/Industry/default.htm.

Sincerely yours,

Courtney H. Lias -S

Courtney H. Lias, Ph.D.
Director
Division of Chemistry and Toxicology Devices
Office of In Vitro Diagnostics
and Radiological Health
Center for Devices and Radiological Health

Enclosure

DEPARTMENT OF HEALTH AND HUMAN SERVICES
Food and Drug Administration

Indications for Use

Form Approved: OMB No. 0910-0120
Expiration Date: January 31, 2017
See PRA Statement below.

510(k) Number *(if known)*
k142129

Device Name
RapidFRET Oral Fluid Assay for Cocaine
RapidFRET Oral Fluid Cocaine Calibrator Set
RapidFRET Oral Fluid Cocaine Control Set

Indications for Use *(Describe)*
The RapidFRET Oral Fluid Assay for Cocaine is a homogeneous time-resolved fluorescence assay that is intended for prescription use in central laboratories only on the RapidFRET Integrated Workstation. The assay is used to perform a qualitative screen for cocaine at 20 ng/mL in neat oral fluid samples collected with the RapidEASE Oral Fluid Collector. This assay is calibrated with Cocaine and provides only a preliminary result. To obtain a confirmed analytical result, a more specific alternate chemical method such as GC/MS or LC/MS/MS is required. Professional judgment should be applied to any drug test result, particularly when using preliminary positive results. For In Vitro Diagnostic Use Only.

The RapidFRET Oral Fluid Cocaine Calibrator Set and RapidFRET Oral Fluid Cocaine Control Set are intended for use with the RapidFRET Oral Fluid Assay for Cocaine and samples collected with the RapidEASE Oral Fluid Collector. The cutoff calibrator is used to determine the cutoff level and translate the assay measurement into a positive or negative result. The positive and negative controls are used to monitor laboratory systems, operators, precision, accuracy and assay conditions. For In Vitro Diagnostic Use Only.

Type of Use *(Select one or both, as applicable)*

☒ Prescription Use (Part 21 CFR 801 Subpart D) ☐ Over-The-Counter Use (21 CFR 801 Subpart C)

PLEASE DO NOT WRITE BELOW THIS LINE – CONTINUE ON A SEPARATE PAGE IF NEEDED.

FOR FDA USE ONLY

Concurrence of Center for Devices and Radiological Health (CDRH) *(Signature)*

510(k) Summary for the RapidFRET Oral Fluid Assay for Cocaine

Preparation Date: July 23, 2015

This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92

The assigned 510(k) number is: k142129

807.92(a)(1): Contact Information

Name: Biophor Diagnostics, Inc.
Address: 1201 Douglas Avenue
Redwood City, CA 94063

Contact: Nathaniel G. Butlin, Ph.D.
Phone: 650-367-4954
Fax: 650-364-4985

807.92(a)(2): Device Name, Common Name and Classification

RapidFRET Oral Fluid Assay for Cocaine (Cocaine Test System)
RapidFRET Oral Fluid Cocaine Calibrator Set (Clinical Toxicology Calibrator)
RapidFRET Oral Fluid Cocaine Control Set (Drug Mixture Control Materials)

Product	Code	Class	Regulation Section	Panel
RapidFRET Oral Fluid Assay for Cocaine	DIO	II	862.3250	91 - Toxicology
RapidFRET Oral Fluid Cocaine Calibrator Set	DLJ	II	862.3200	91 - Toxicology
RapidFRET Oral Fluid Cocaine Control Set	DIF	I, Reserved	862.3280	91 - Toxicology

807.92(a)(3): Identification of Legally Marketed Predicate Devices

CEDIA® Cocaine OFT Assay (k101742) marketed by Microgenics Corporation, Thermo Fisher Scientific Clinical Diagnostic Division.

807.92(a)(4): Device Description

The RapidFRET Oral Fluid Assay for Cocaine is an In Vitro Diagnostic competitive immunoassay used to detect cocaine in human oral fluid. This is a ready-to-use homogenous system that involves energy transfer between an acceptor fluorophore labeled to an antibody and a donor fluorophore labeled to drug. The assay is based on competition between drug in the sample and drug labeled with the donor fluorophore for a fixed number of binding sites on the antibody reagent. When acceptor and donor fluorophores are brought into close proximity through a binding event, energy transfer occurs. The fluorescence resonance energy transfer (FRET) signal is measured at the wavelength of the

acceptor fluorophore and is inversely proportional to the amount of drug in the sample. A Cutoff Calibrator is used to translate the sample measurement into a positive or negative result. Controls are used to establish and monitor precision and accuracy.

807.92(a)(5): Intended Use

The RapidFRET Oral Fluid Assay for Cocaine is a homogeneous time-resolved fluorescence assay that is intended for prescription use in central laboratories only on the RapidFRET Integrated Workstation. The assay is used to perform a qualitative screen for cocaine at 20 ng/mL in neat oral fluid samples collected with the RapidEASE Oral Fluid Collector. This assay is calibrated with Cocaine and provides only a preliminary result. To obtain a confirmed analytical result, a more specific alternate chemical method such as GC/MS or LC/MS/MS is required. Professional judgment should be applied to any drug test result, particularly when using preliminary positive results. For In Vitro Diagnostic Use Only.

The RapidFRET Oral Fluid Cocaine Calibrator Set and RapidFRET Oral Fluid Cocaine Control Set are intended for use with the RapidFRET Oral Fluid Assay for Cocaine and samples collected with the RapidEASE Oral Fluid Collector. The cutoff calibrator is used to determine the cutoff level and translate the assay measurement into a positive or negative result. The positive and negative controls are used to monitor laboratory systems, operators, precision, accuracy and assay conditions. For In Vitro Diagnostic Use Only.

807.92(a)(6): Technological Similarities and Differences to the Predicate

	Candidate Device (RapidFRET COC)	**Predicate Device (Microgenics COC, K101742)**
Indications for Use	Qualitative determination of cocaine in human oral fluid in clinical setting.	Qualitative determination of cocaine in human oral fluid in clinical setting.
Methodology	Competitive homogeneous immunoassay.	Competitive homogeneous immunoassay.
Kit Components	1 Drug specific antibody reagent in liquid, ready to use format. 1 Drug conjugate reagent in liquid, ready to use format.	1 Drug specific antibody reagent (marketed in combination as a lyophilized reagent and reconstitution buffer). 1 Drug conjugate reagent (marketed in combination as a lyophilized reagent and reconstitution buffer).
Performance Characteristics	Precision, accuracy, cross reacting/interfering studies demonstrate equivalence to the predicate device.	Precision, accuracy, cross reacting/interfering studies are similar to the RapidFRET Oral Fluid Assay for Cocaine.
Safety and	Demonstrated in bench testing and	Demonstrated in bench testing and

	Candidate Device (RapidFRET COC)	**Predicate Device (Microgenics COC, K101742)**
Effectiveness	described in PI, equivalent to predicate.	described in PI.
Neat Oral Fluid Cutoff Level	20 ng/mL neat oral fluid.	15 ng/mL neat oral fluid using a 5 ng/mL cutoff calibrator to account for sample dilution by collection device.
Platform	RapidFRET Integrated Workstation available exclusively from Biophor Diagnostics, Inc.	MGC240 analyzer
Sample Collection	Neat oral fluid is collected with the RapidEASE Oral Fluid Collector via direct expectoration. No diluent is used and sample is stored in glass sample tube with inert screw cap.	Oral fluid is collected with the Oral-Eze Saliva Collection System. This device uses an absorbent swab and diluent. Sample is stored in plastic tube with snap cap.
Principle and Procedure	Drugs in the oral fluid sample compete with the drug conjugate donor fluorophore for a fixed number of binding sites on the individual drug antibody acceptor reagents. When acceptor and donor fluorophores are brought into close proximity, through the binding event, fluorescent energy transfer is measured. The amount of drug in the specimen sample is inversely proportional to the assay signal as measured by time resolved fluorescence.	The assay is based on the sample analytes competing with analyte conjugates to one inactive fragment of β-galactosidase for antibody binding sites. The amount of drug in the specimen is proportional to the assay signal as measured by absorbance.
Controls and Calibrator Levels	Calibrators are available at effective concentrations of 0 ng/mL and 20 ng/mL. Controls are available at effective concentrations of 10 ng/mL and 30 ng/mL.	Calibrators are available at 0 ng/mL, 5 ng/mL, and 50 ng/mL. Controls are available at additional levels.

807.92(b)(1): Brief Description of Study Data:

A series of studies were performed that evaluated the device performance characteristics including precision and analytical sensitivity, correlation with GC/MS and LC/MS/MS, cross reactivity, and analytical specificity that are summarized below.

Precision and Analytical Sensitivity

One lot of RapidFRET Oral Fluid Assay for Cocaine was used to verify precision, four times daily, triplicate samples per run for 5 days using 3 independent lots of reagent. Negative oral fluid pools were spiked with cocaine at 0%, 25%, 50%, 75%, 100%, 125%, 150%, 175% and 200% of the cutoff level corresponding to approximately 0, 5, 10, 15, 20, 25, 30, 35 and 40

ng/mL. The aggregate data is summarized in the table below:

Summary Precision Data for All Lots									
	0%	25%	50%	75%	100%	125%	150%	175%	200%
POS	0	0	0	1	86	171	180	180	180
NEG	180	180	180	179	94	9	0	0	0
N	180	180	180	180	180	180	180	180	180

Summary Precision Data for All Lots: Percent Agreement									
	0%	25%	50%	75%	100%	125%	150%	175%	200%
POS	0%	0%	0%	1%	48%	95%	100%	100%	100%
NEG	100%	100%	100%	99%	52%	5%	0%	0%	0%
N	180	180	180	180	180	180	180	180	180

The data indicate that the analytical sensitivity is between 75% and 125% of cutoff, and expected results were achieved at a 97% frequency within this range.

Correlation with MS Quantitation

Neat oral fluid was collected with the RapidEASE Oral Fluid Collection Device from volunteers potentially positive and negative for opiates. The samples (n=294) were randomized and blinded to the instrument operator and assayed using RapidFRET COC reagents. Following screening, positive and negative samples were sent for confirmatory testing. The summarized data are shown below.

n = 294	Low Negative (<10 ng/mL)	Near Cutoff Negative (10 - 20 ng/mL)	Near Cutoff Positive (20 – 30 ng/mL)	High Positive (>30 ng/mL)
RapidFRET POS	1[§]	2[§]	5	55
RapidFRET NEG	226	5	0	0

[§]One sample contained cinnamoyl cocaine at 388 ng/mL; a second sample contained cocaine, benzoylecgonine, and cinnamoyl cocaine at 10 ng/mL equivalent concentration; a third sample contained high levels of hydroxymethoxymethcathinone (HMMC), a major metabolite of methylone, which shares structural similarities to isoxsuprine, a known cross-reactant.[1]

The data indicate that the RapidFRET Oral Fluid Assay for Cocaine was accurate >99% of the time in neat oral fluid samples collected with the RapidEASE Oral Fluid Collector.

Cross Reactivity and Analytical Specificity

A compound library of approximately 171 different structurally related and unrelated compounds including metabolites, OTC and prescription medications and drugs of abuse was used to evaluate the device cross reactivity and specificity. Compounds were spiked at 30,000 ng/mL into neat oral fluid pool aliquots with 0 ng/mL, 10 ng/mL and 30 ng/mL of cocaine, processed with the RapidEASE Collector, and tested with the RapidFRET COC assay. Those compounds that gave an unexpected result were further titrated to determine the concentration at which the cross-reacting compound yielded a result approximately

[1] Kamata et al., *Japanese Journal of Forensic Science and Technology*, (2007), 12(1):97-106. Ellefsen, Kayla N., et al., *Forensic Toxicology* (2015): 1-11.

equivalent to the cutoff. Thirteen (13) structurally related compounds were determined to cross-react below 30,000 ng/mL in the absence of cocaine. These are noted in the labeling.

Compound	Concentration (ng/mL)	Cross-Reactivity (%)
Benzoylecgonine	18	111%
Chlorpromazine	17,705	0.1%
Cinnamoylcocaine	224	8.2%
Clomipramine	13,824	0.1%
Cocaethylene	15	133%
Cocaine	20.5	98%
Cyclobenzaprine	18,218	0.1%
Ecgonine	3,384	0.6%
Ecgonine methyl ester	3,365	0.6%
Imipramine	19,847	0.1%
Isoxsuprine*	846	2.4%
Norcocaine	1,730	1.2%
Perphenazine	5,959	0.3%
Thioridazine	23,723	0.1%
Trifluoperazine	21,831	0.1%

*Hydroxymethoxymethcathinone (HMMC), a major metabolite of methylone, shares structural similarities to isoxsuprine and has been shown to cause interference.

A second study evaluated common substances such as foods and dental products as well as pH variations. HSA, ethanol, baking soda, whole blood, hemoglobin, hydrogen peroxide, sodium chloride, cholesterol, denture adhesive, ascorbic acid, bilirubin, IgA, IgG and IgM were spiked into neat oral fluid pool aliquots that contained either 10 ng/mL or 30 ng/mL of cocaine. Neat oral fluid pool was titrated to pH values of 5, 6, 7, 8 and 9, spiked with cocaine to 10 ng/mL or 30 ng/mL and assayed with the RapidFRET COC Assay. The effects of antiseptic mouthwash, cough syrup, cranberry juice, orange juice, tooth paste, chewing tobacco, cigarettes, chewing gum, hard candy, teeth whitening strips, cola, water, antacid, coffee and tea were evaluated by asking volunteers to use a specific item and provide an oral fluid sample. These samples were then spiked with cocaine to 10 ng/mL or 30 ng/mL, processed with a RapidEASE Collector and assayed with the RapidFRET COC device. All compounds at the listed concentrations gave a NEG result when spiked with 10 ng/mL cocaine and a POS result when spike with 30 ng/mL cocaine.

807.92(b)(3): Conclusions

The RapidFRET Oral Fluid Assay for Cocaine including the RapidFRET Oral Fluid Negative and Cutoff Calibrators, the RapidFRET Oral Fluid Negative and Positive Controls and the RapidEASE Oral Fluid Collector were determined to be safe and effective for their intended use.